REMARKS

Claims 1-6 and 10-12 are currently pending and stand rejected.

Claims 1, 5 and 6 have been amended. Support for the amendments to claim 1, 5 and 6 can be found at specification at page 18 lines 15-33, page 19, lines 12-14, page 20, lines 7-13, page 22, lines 23-25, page 52, lines 21-31, and throughout the specification. No new matter has been added by the amendments.

The Office Action withdrew all previous rejections under 35 U.S.C. §112, first paragraph for new matter, as well as the previous rejection under 35 U.S.C. §112, second paragraph, (see Office Action, page 2, paragraph 2).

Please reconsider the Application in light of the following remarks.

I. The Claims Meet the Requirements of 35 U.S.C. § 112, First Paragraph

Claim 1 and dependent claims 2-6 and 10-12 stand rejected under 35 U.S.C. § 112, first paragraph, for an alleged insufficient written description to show that Applicants were in possession of a "factor" in which to culture pluripotential cells which would cause them to express characteristics of DCs (Office Action, page 2, part 4).

Claim 1 has been amended to delete the term "a factor", and to specify that "a composition selected from the group consisting of peripheral blood mononuclear cell conditioned medium, monocyte conditioned medium, macrophage conditioned medium or fixed Staphylococcus aureus Cowan 1 strain (SACS)" is added to the immature dendritic cells produced in step (a). Dependent claims 5 and 6 have been amended to delete the term "the factor" and instead refer to "the composition" specified in claim 1. Support for adding peripheral blood mononuclear cell conditioned medium or monocyte conditioned medium to the immature DCs produced in step (a) can be found in the specification at page 18 lines 15-33, page 19, lines 12-14, and throughout the specification. Support for adding macrophage conditioned medium to the immature DCs produced in step (a) can be found in the specification at page 22, lines 23-25. Support for adding SACS to the immature DCs produced in step (a) can be found in the specification at page 20, lines 7-13 and page 52, lines 21-31. Accordingly, Applicants respectfully submit that this rejection of claims 1-6 and 10-12 under 35 U.S.C. §112, first paragraph, may be properly withdrawn.

Claim 1 and dependent claims 2-6 and 10-12 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter with respect to the recitation in claim 1 of "macrophage conditioned medium" (Office Action, page 5, part 9).

Applicants respectfully traverse this rejection. Support for the maturation of immature DCs to mature DCs by the addition of macrophage conditioned medium can be found in the specification at page 22, lines 23-25 of the specification. Accordingly, no new matter has been added, and this rejection under 35 U.S.C. § 112, first paragraph, may be properly withdrawn.

II. The Claims Meet the Requirements of 35 U.S.C. § 112, Second Paragraph

Claims 1-6 and 10-12 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite (Office Action at page 5, part 11). The Office Action alleges that the recitation in claim 1 of: "A method for producing dendritic cells" resulting in "stable mature dendritic cells" is vague and indefinite, as the result of the method does not match the preamble of the claim.

According to the Examiner's advice, Applicants have amended the preamble of claim 1, to recite "A method of producing stable mature dendritic cells". Thus, the preamble of claim 1 now matches the result of the claimed method. Accordingly, the rejection under 35 U.S.C. § 112, second paragraph, may be properly withdrawn.

III. The Claims Meet the Requirements of 35 U.S.C. § 102.

Claim 1 and dependent claims 2-6 and 10-12 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent No. 5,994,126, as evidenced by Kiertscher (Office Action at page 3, part 6). According the to Office Action, the '126 patent teaches an *in vitro* method of producing DCs comprising culturing pluripotential cells comprising monocytes or mononuclear cells (both components of PBMCs) in GM-CSF and IL-4 to produce DCs with increased CD83, as evidenced by Kiertscher. In particular, the Office Action states that there is no limitation in claim 1 that step (b) must follow step (a) in any particular time frame, and alleges that the continuous culture conditions described in the '126 patent meet the limitations of the claims.

Applicants have amended claims 1 to further clarify that the method of the invention is a two step process. Step (b) of claim 1 now specifies that peripheral blood mononuclear cell

conditioned medium, monocyte conditioned medium, macrophage conditioned medium or fixed Staphylococcus aureus Cowan 1 strain (SACS) is added to the immature dendritic cells produced in step (a). Thus, claim 1 specifies: a) a first step of contacting pluripotential cells with one or more cytokines for a time sufficient to produce immature DCs, and b) a second step of adding one of the above mentioned condition media or SACS to the immature DCs produced in step (a) and culturing for a time sufficient to produce stable mature dendritic cells. Support for the amendment is described at page 4 of this paper.

This two step process specified in claim 1 is not disclosed by the '126 patent. Rather, the '126 patent discloses the continuous culture of pluripotential cells induced to differentiate into (unstable) dendritic cells with a cytokine (such as GM-CSF), but does not disclose the addition of conditioned medium or SACS to such dendritic cells, as is specified in step (b) of amended claim 1.

Furthermore, the continuous culture conditions disclosed by the '126 patent do not result in the production of stably mature dendritic cells. The legend to Figure 6 on pages 10-11 of the instant specification compares the continuous culture method of the '126 patent (continuous culture in GM-CSF and IL-4 for days 1-10), and then 3 days of cytokine-free culture, to the two step method of the instant invention (culture in GM-CSF plus IL-4 for days 1-6, followed by the second step of adding conditioned media at day 7 and culture for three days (days 7-10)), and then 3 days of cytokine-free culture. Figure 6 shows that after 3 days of cytokine-free culture, the cell cultured according to the continuous culture method of the '126 patent have the appearance of macrophages (Figure 6A, upper left panel). Thus, the DC produced by the one step continuous culture method of the '126 patent are unstable and revert to a macrophage phenotype after three days of cytokine free culture. In contrast, the DCs produced by the two step method of the invention are stably mature, as evidenced by the retention of the DC phenotype after three days of cytokine-free culture (Figure 6C-D, lower left and right panels).

As described above, the two step method specified in amended claim 1 and dependent claims 2-6 and 10-12 are not anticipated by the continuous culture method of '126 patent. Accordingly, the rejection of claim 1 and dependent claims 2-6 and 10-12 under 35 U.S.C. §102(e) may be properly withdrawn.

Claim 1 and dependent claims 2-6 and 10-12 stand rejected under 35 U.S.C. §102(b) as

allegedly anticipated by Romani et al., J. Exp. Med. 180: 83-93, 1994 ("Romani"), as evidenced by Caux et al. (Office Action at page 4, part 7). The basis of this rejection is similar to that of the 102(e) rejection, above. The Office Action alleges that culture of pluripotential cells for 5-7 days as described by Romani to produce DCs with increased CD83 and CD86 expression anticipates the pending claims.

As described above, claim 1 has been amended to recite a two step process, where step (b) specifies that peripheral blood mononuclear cell conditioned medium, monocyte conditioned medium, macrophage conditioned medium or fixed Staphylococcus aureus Cowan 1 strain (SACS) is added to the immature dendritic cells produced in step (a). The addition of the specified conditioned medium or SACS in step (b) results in the maturation of immature DC to stable mature DC. In contrast, Romani does *not* disclose the second step of *adding* peripheral blood mononuclear cell conditioned medium, monocyte conditioned medium, macrophage conditioned medium or SACS to DC. Similarly to the DCs produced by the method of the '126 patent, the DCs produced by the Romani method are immature dendritic cells that, once removed from the cytokines used to produce them, revert to a macrophage phenotype. It is the novel addition of peripheral blood mononuclear cell conditioned medium, monocyte conditioned medium, macrophage conditioned medium or SACS to immature DC, as specified in step (b) of claim 1 that results in the maturation of these immature dendritic cells into stable mature dendritic cells. Thus, amended claim 1 and dependent claims 2-6 and 10-12 are novel and unanticipated by Romani. Accordingly, the rejection under 35 U.S.C. §102(b) may be properly withdrawn.

CONCLUSION

Applicants respectfully submit that the claims are in condition for allowance. However, if the Examiner believes that any further discussion of this communication would be helpful, he is encouraged to contact the undersigned by telephone.

No fees are believed to be due in connection with this communication. Should any addition charges be due, please apply them to our Deposit Account No. 50-3187.

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